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Medical Focus - Avian Flu Essentials

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“Based on our results, combinations of mitigation strategies such as stockpiling vaccines or antiviral agents, along with social distancing measures could be particularly effective in slowing pandemic flu spread in the U.S.”

– Dr. Ira Longini, a biostatistician at the Fred Hutchinson Cancer Research Center and the University of Washington School of Public Health and Community Medicine

Dear Colleague:

In the twenty-second letter of the Avian Flu Essentials series, I plan to give more details on how antiviral drugs work and why the use of these medications can help mitigate the impact of a potential pandemic. The Department of Health and Human Services is making progress towards procuring enough antiviral drugs for 25 percent of the US population.

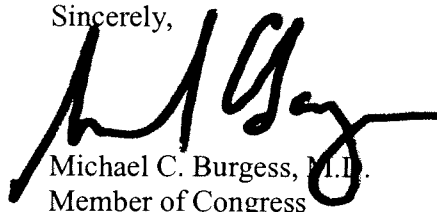
Four drugs can currently be used for prophylaxis or treatment against influenza. These fall into two classes of drugs. One class, the adamantanes (amantadine and rimantadine), decrease the amount of virus made by inhibiting the virus from shedding its coat. In addition, this class can only be used against influenza A, which mainly circulates in animals. The other types of influenza include influenza B, which is most often found in humans, and influenza C, which just causes minor illness.

Resistance to adamantanes has sharply increased over the last year. Therefore, the CDC has recommended against the use of this class of drugs for this influenza season to prevent adamantane-resistant influenza from spreading.

The second class of antiviral drugs is neuraminidase inhibitors (zanamivir/Relenza and oseltamivir/Tamiflu). Unlike the adamantanes, these drugs are still effective against influenza and work by stopping new viruses from being released from infected cells. Neuraminidase inhibitors can also be used against all strains of influenza. According to a study reviewed in the New England Journal of Medicine, “oseltamivir treatment reduced the median duration of illness by more than 30 percent (from 4.3 days to 3 days) and the severity of illness by about 40 percent.” Another study showed that the early administration of Tamiflu “within the first 12 hours after the onset of fever shortened the illness by more than three days, as compared with treatment that was started at 48 hours.”

This data supports the fact that the severity of illness is decreased with the use of neuraminidase inhibitors and this is significant to decrease complications associated with the flu. An article on the reverse of this letter describes how antivirals, such as Tamiflu and Relenza, in essence can provide us time by assisting in the containment of the disease and allowing a vaccine specific to the actual pandemic viral strain to be manufactured.

Sincerely,


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Excerpt from a National Institute of General Medical Sciences press release, *Computer Model Examines Strategies to Mitigate Potential U.S. Flu Pandemic*, April 3, 2006:

If pandemic flu were to emerge in the United States, what interventions might slow its spread and minimize the impact? With support from the National Institutes of Health (NIH), researchers from the Fred Hutchinson Cancer Research Center in Seattle, Wash., and the Los Alamos National Laboratory have used computer models to suggest possible answers. The findings appear in the April 11, 2006, issue of the *Proceedings of the National Academy of Sciences* and will be available in the online edition the week of April 3.

By developing a model that represents the U.S. population and tests different properties of a potential pandemic flu virus, the researchers evaluated the effectiveness of different intervention strategies. They found that, depending on the contagiousness of the virus, a variety of approaches could reduce the number of cases to less than that of an annual flu season.

“Preparing for a potential pandemic is tremendously challenging, given the potential scope and the large number of unknowns,” said NIH Director Elias A. Zerhouni, M.D. “The best approach is to use all of the tools available to us, including computer modeling. By predicting the impact of intervention strategies, these models can help health officials and policymakers plan for a real pandemic.”

The recent modeling work is part of an ongoing research program called the Models of Infectious Disease Agent Study (MIDAS), supported by NIH’s National Institute of General Medical Sciences (NIGMS). Researchers in the network develop computer models to better understand the spread of infectious diseases, whether they occur naturally or deliberately. With growing concerns that the H5N1 strain of the avian flu virus, initially found in birds throughout Southeast Asia, could eventually be transmitted easily between people, the research network has been modeling pandemic flu in different parts of the world.

“The MIDAS researchers previously developed models of a potential pandemic flu outbreak in Thailand and surrounding areas that showed containment at the source is feasible,” explained Jeremy M. Berg, Ph.D., NIGMS director. “But we need to consider the possibility that if the outbreak isn’t contained, it could quickly spread globally.”

Using data from the 2000 U.S. Census and the U.S. Department of Transportation, the researchers developed a model that represents the demographics and travel patterns of 281 million people living in the United States. They also incorporated information about the potential virus based on previous flu pandemics, including different assumptions about its possible contagiousness (but not its potential effects on mortality). The researchers then introduced a small number of hypothetical travelers, who are infected but not yet symptomatic, arriving daily at 14 major U.S. international airports. With these assumptions in place, the scientists simulated a virtual outbreak on high-performance computers at the Los Alamos National Laboratory.

“The goal for the U.S. modeling project was to determine how to slow spread long enough so that a well-matched vaccine could be developed and distributed,” said the research team’s leader, Ira M. Longini, Jr., Ph.D., a biostatistician at the Fred Hutchinson Cancer Research Center and the University of Washington School of Public Health and Community Medicine. An additional guideline was to reduce the number of overall cases to or below 10 percent of the population, the average percentage reported during an annual flu season.

To identify such measures, the researchers tested different interventions: distributing antiviral treatments to infected individuals and others near them to reduce symptoms and susceptibility; vaccinating people, possibly children first, with either one or two shots of a vaccine not well matched to the strain that may emerge; social distancing, such as restricting travel and quarantining households; and closing schools.

The results showed that with no intervention a pandemic flu with low contagiousness could peak after 117 days and infect about 33 percent of the U.S. population. A highly contagious virus could peak after 64 days and infect about 54 percent of people.

The researchers then compared what might happen in scenarios involving the use of different interventions. When the simulated virus was less contagious, the three most effective single measures included distributing several million courses of antiviral treatment to targeted groups seven days after a pandemic alert, school closures, and vaccinating 10 million people per week with one dose of a poorly matched vaccine. The results also showed that vaccinating school children first is more effective than random vaccination when the vaccine supply is limited. Regardless of contagiousness, social distancing measures alone had little effect.

But when the virus was highly contagious, all single intervention strategies left nearly half the population infected. In this instance, the only measures that reduced the number of cases to below the annual flu rate involved a combination of at least three different interventions, including a minimum of 182 million courses of antiviral treatment.